

## APPENDIX

Claim 6. (Amended) A process for selecting a suitable signal peptide for secretory expression of a desired protein in *E. coli*, comprising:

- (a) expression in *E. coli* in culture medium, hirudin or a hirudin derivative which has antithrombotic activity, and which has a defined amino acid, aa<sub>x</sub>, at its N terminus, wherein said amino acid aa<sub>x</sub> is connected via its N-terminal to a signal peptide to be tested;
- (b) determining expression rate by measuring said hirudin or hirudin derivative [protein] activity in the culture supernatant;
- (c) repeating steps (a) and (b) with various signal peptides;
- (d) selecting said suitable signal peptide by comparing the expression rates represented by the hirudin antithrombotic activity found in step (b).

Claim 8. (Amended) The process of claim 6, further comprising expressing said suitable signal peptide and the desired protein in *E. coli* via a nucleic acid construct, wherein [expression] secretion of the desired protein and said suitable peptide occurs with simultaneous elimination of said suitable signal peptide.